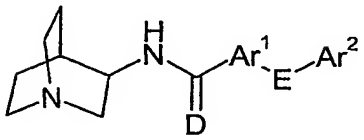
CLAIMS

1. A compound having low P-glycoprotein-mediated efflux according to formula I:



I

wherein:

D represents oxygen or sulfur;

E represents a single bond, oxygen, sulfur, or NR^1;

Ar^1 is selected from an ortho-substituted 5- or 6-membered aromatic or heteroaromatic ring having 0, 1 or 2 nitrogen atoms, 0 or 1 oxygen atoms, and 0 or 1 sulfur atoms, or selected from an ortho-substituted 8-, 9- or 10-membered fused aromatic or heteroaromatic ring system having 0, 1, 2 or 3 nitrogen atoms, 0 or 1 oxygen atoms, and 0 or 1 sulfur atoms, said aromatic or heteroaromatic rings or ring systems having ortho-substituents selected from -C_1-C_6alkyl, -C_2-C_6alkenyl, -C_2-C_6alkynyl, halogen, -CN, -NO_2, -CF_3, -$S(O)_nR^2$, -NR^2R^3, -$CH_2NR^2R^3$, -OR^2, -CH_2OR^2 or -CO_2R^4;

Ar^2 is selected from a 5- or 6-membered aromatic or heteroaromatic ring having 0, 1 or 2 nitrogen atoms, 0 or 1 oxygen atoms, and 0 or 1 sulfur atoms;

where Ar^2 is unsubstituted or has 1, 2 or 3 substituents independently selected from -R^2, -C_1-C_6alkyl, -C_2-C_6alkenyl, -C_2-C_6alkynyl, halogen, -CN, -NO_2, -CF_3, -$S(O)_nR^2$, -NR^2R^3, -$CH_2NR^2R^3$, -OR^2, -CH_2OR^2 or -CO_2R^4;

R^2 and R^3 are independently selected at each occurrence from hydrogen, -C_1-C_4alkyl, aryl, heteroaryl, -$C(O)R^4$, -$C(O)NHR^4$, -CO_2R^4 or -SO_2R^4, or

R^2 and R^3 in combination is -$(CH_2)_jG(CH_2)_k$- wherein G is oxygen, sulfur, NR^4, or a bond;

j is 2, 3 or 4;

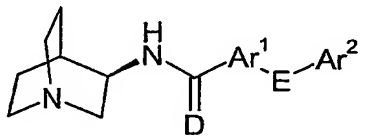
k is 0, 1 or 2;

n is 0, 1 or 2, and

R^4 is independently selected at each occurrence from hydrogen, -C_1-C_4alkyl, aryl, or heteroaryl, and

stereoisomers, enantiomers, *in vivo*-hydrolysable precursors and pharmaceutically-acceptable salts thereof.

2. A compound according to Claim 1 being an R-isomers of a compound of formula I in accord with formula II,



II

wherein D, Ar^1, E and Ar^2 are as defined for compounds of formula I.

3. A compound according to Claim 1, wherein:

D represents oxygen or sulfur;

E represents a single bond, oxygen, sulfur, or NR^1;

Ar^1 is selected from an ortho-substituted 5- or 6-membered aromatic or heteroaromatic ring having 0, 1 or 2 nitrogen atoms, 0 or 1 oxygen atoms, and 0 or 1 sulfur atoms, or selected from an ortho-substituted 8-, 9- or 10-membered fused aromatic or heteroaromatic ring system having 0, 1, 2 or 3 nitrogen atoms, 0 or 1 oxygen atoms, and 0 or 1 sulfur atoms, said aromatic or heteroaromatic rings or ring systems having ortho-substituents selected from -C_1-C_6alkyl, halogen, -CN, -NO_2, -CF_3, -NR^2R^3, -OR^2, or -CO_2R^4;

Ar^2 is selected from a 5- or 6-membered aromatic or heteroaromatic ring having 0, 1 or 2 nitrogen atoms, 0 or 1 oxygen atoms, and 0 or 1 sulfur atoms;

where Ar^2 is unsubstituted or has 1, 2 or 3 substituents independently selected from -R^2, -C_1-C_6alkyl, -C_2-C_6alkenyl, -C_2-C_6alkynyl, halogen, -CN, -NO_2, -CF_3, -$S(O)_nR^2$, -NR^2R^3, -$CH_2NR^2R^3$, -OR^2, -CH_2OR^2 or -CO_2R^4;

R^2 and R^3 are independently selected at each occurrence from hydrogen, -C_1.C_4alkyl, aryl, heteroaryl, -$C(O)R^4$, -$C(O)NHR^4$, -CO_2R^4 or -SO_2R^4, or

R^2 and R^3 in combination is -$(CH_2)_jG(CH_2)_k$- wherein G is oxygen, sulfur, NR^4, or a bond;

j is 2, 3 or 4;

k is 0, 1 or 2;

n is 0, 1 or 2, and

R^4 is independently selected at each occurrence from hydrogen, -C_1-C_4alkyl, aryl, or heteroaryl, and

stereoisomers, enantiomers, *in vivo*-hydrolysable precursors and pharmaceutically-acceptable salts thereof.

4. A compound according to Claim 1, wherein:

D represents oxygen;

E represents a single bond;

Ar^1 is selected from an ortho-substituted 5- or 6-membered aromatic or heteroaromatic ring having 0, 1 or 2 nitrogen atoms, 0 or 1 oxygen atoms, and 0 or 1 sulfur atom, said aromatic or heteroaromatic rings or having ortho-substituents selected from -C_1-C_6alkyl, halogen, -CN, -NO_2, -CF_3, -NR^2R^3, -OR^2 or -CO_2R^4;

Ar^2 is selected from a 5- or 6-membered aromatic or heteroaromatic ring having 0, 1 or 2 nitrogen atoms, 0 or 1 oxygen atoms, and 0 or 1 sulfur atoms, and

stereoisomers, enantiomers, *in vivo*-hydrolysable precursors and pharmaceutically-acceptable salts thereof.

5. A compound according to Claim 1, wherein:

D represents oxygen;

E represents a single bond;

Ar^1 is selected from an ortho-substituted 5- or 6-membered aromatic or heteroaromatic ring having 0, 1 or 2 nitrogen atoms, 0 or 1 oxygen atoms, and 0 or 1 sulfur atom, said aromatic or heteroaromatic ring having ortho-substituents selected from -CN, -NO_2, -CF_3, or -OR^2;

Ar^2 is selected from phenyl or pyridyl, and

stereoisomers, enantiomers, *in vivo*-hydrolysable precursors and pharmaceutically-acceptable salts thereof.

6. A compound according to Claim 1, wherein:

D is O; or an enantiomer thereof, and pharmaceutically-acceptable salts thereof.

7. A compound according to Claim 1, wherein:

Ar^1 is selected from phenyl or thiophenyl and Ar^2 is selected from phenyl, pyridyl, furanyl or thiophenyl having optional substituents as defined herein.

8. A compound according to Claim 1, selected from:
N-(R)-1-Azabicyclo[2.2.2]oct-3-yl-2-methyl-5-phenylbenzamide;
N-(R)-1-Azabicyclo[2.2.2]oct-3-yl-2-methyl-3-phenylbenzamide;
(N-(R)-1-Azabicyclo[2.2.2]oct-3-yl)-3-methyl-5-phenylthiophene-2-carboxylic acid amide;
(N-(R)-1-Azabicyclo[2.2.2]oct-3-yl)-3-methyl-5-(3-pyridyl)thiophene-2-carboxylic acid amide;
N-(R)-1-Azabicyclo[2.2.2]oct-3-yl-2-carboxy-5-phenylbenzamide;
N-(R)-1-Azabicyclo[2.2.2]oct-3-yl-2-carboxy-3-phenylbenzamide;
(N-(R)-1-Azabicyclo[2.2.2]oct-3-yl)-3-carboxy-5-phenylthiophene-2-carboxylic acid amide;
(N-(R)-1-Azabicyclo[2.2.2]oct-3-yl)-3-carboxy-5-(3-pyridyl)thiophene-2-carboxylic acid amide;
N-(R)-1-Azabicyclo[2.2.2]oct-3-yl-2-cyano-5-phenylbenzamide;
N-(R)-1-Azabicyclo[2.2.2]oct-3-yl-2-cyano-3-phenylbenzamide;
(N-(R)-1-Azabicyclo[2.2.2]oct-3-yl)-3-cyano-5-phenylthiophene-2-carboxylic acid amide;
(N-(R)-1-Azabicyclo[2.2.2]oct-3-yl)-3-cyano-5-(3-pyridyl)thiophene-2-carboxylic acid amide;
N-(R)-1-Azabicyclo[2.2.2]oct-3-yl-2-amino-5-phenylbenzamide;
N-(R)-1-Azabicyclo[2.2.2]oct-3-yl-2-amino-3-phenylbenzamide;
(N-(R)-1-Azabicyclo[2.2.2]oct-3-yl)-3-amino-5-phenylthiophene-2-carboxylic acid amide, or
(N-(R)-1-Azabicyclo[2.2.2]oct-3-yl)-3-amino-5-(3-pyridyl)thiophene-2-carboxylic acid amide.
or pharmaceutically-acceptable salts thereof.

9. A method of treatment or prophylaxis of a disease or condition in which activation of the α7 nicotinic receptor is beneficial which method comprises administering a therapeutically-effective amount of a compound according to Claim 1 to a subject suffering from said disease or condition.

10. The method of Claim 9, wherein said disease or condition is anxiety, schizophrenia, mania or manic depression.

11. A method of treatment or prophylaxis of neurological disorders, psychotic disorders or intellectual impairment disorders, which comprises administering a therapeutically effective amount of a compound according to Claim 1.

12. The method of Claim 11, wherein said disorder is Alzheimer's disease, learning deficit, cognition deficit, attention deficit, memory loss, Attention Deficit Hyperactivity Disorder, Parkinson's disease, Huntington's disease, Tourette's syndrome, neurodegenerative disorders in which there is loss of cholinergic synapses, jetlag, nicotine addiction, craving, pain, or ulcerative colitis.

13 A method for inducing the cessation of smoking comprising administering an effective amount of a compound according to Claim 1.

14. A pharmaceutical composition comprising a compound according to Claim 1 and a pharmaceutically-acceptable diluent, lubricant or carrier.

15. A method of treatment or prophylaxis of a disease or condition in which activation of the $\alpha 7$ nicotinic receptor is beneficial which method comprises administering a therapeutically-effective amount of a pharmaceutical composition according to Claim 14 to a subject suffering from said disease or condition.

16. The method of Claim 15, wherein said disease or condition is anxiety, schizophrenia, mania or manic depression.

17. A method of treatment or prophylaxis of neurological disorders, psychotic disorders or intellectual impairment disorders, which comprises administering a therapeutically effective amount of a pharmaceutical composition according to Claim 14.

18. The method of Claim 15, wherein said disorder is Alzheimer's disease, learning deficit, cognition deficit, attention deficit, memory loss, Attention Deficit Hyperactivity Disorder, Parkinson's disease, Huntington's disease, Tourette's syndrome, neurodegenerative

disorders in which there is loss of cholinergic synapses, jetlag, nicotine addiction, craving, pain, and for ulcerative colitis.

19. A method for inducing the cessation of smoking comprising administering an effective amount of a pharmaceutical composition according to Claim 14.

20. The use of a compound according to Claim 1, an enantiomer thereof or a pharmaceutically-acceptable salt thereof, in the manufacture of a medicament for the treatment or prophylaxis of human diseases or conditions in which activation of the $\alpha 7$ nicotinic receptor is beneficial selected from neurological disorders, psychotic disorders, intellectual impairment disorders, Alzheimer's disease, learning deficit, cognition deficit, attention deficit, memory loss, Attention Deficit Hyperactivity Disorder, anxiety, schizophrenia, mania or manic depression, Parkinson's disease, Huntington's disease, Tourette's syndrome, or neurodegenerative disorders in which there is loss of cholinergic synapses.